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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/813,177	GU ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-60* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-8, as specifically drawn to a method of determining whether a subject has neoplasia comprising assaying a diagnostic sample of the subject for Mdm2 expression and HAUSP expression, wherein the sample is diagnosed using an antibody which is reactive with MDM2 and an antibody reactive with HAUSP, classified in class 435, subclass 7.1.

II. Claims 1-5 and 9-11, as specifically drawn to a method of determining whether a subject has neoplasia comprising assaying a diagnostic sample of the subject for Mdm2 expression and HAUSP expression, wherein the sample is assayed using a nucleic acid probe which hybridizes to nucleic acid encoding Mdm2 and a nucleic acid probe which hybridizes to nucleic acid encoding HAUSP, classified in class 435, subclass 6.

III. Claims 12-15, as specifically drawn to a method of assessing the efficacy of therapy to treat neoplasia who has undergone or is undergoing treatment for neoplasia, comprising assaying a diagnostic sample of the subject for Mdm2 expression and HAUSP expression, classified in class 435, subclass 4.

IV. Claims 16-17, as specifically drawn to a kit for use in detecting neoplasia, comprising at least one agent reactive with Mdm2 and at least one agent reactive with HAUSP, classified in class 435, subclass 810.

V. Claims 18-23, 35-46 and 51-52, as specifically drawn to a method for treating neoplasia in a subject, comprising increasing the activity of p53 in a subject, wherein the activity of p53 is increased in the subject by modulating Mdm2-HAUSP

interaction in the subject, classified in class 424, subclass 130.1 and class 514, subclass 2.

VI. Claims 24-34, as specifically drawn to a method for debiquitinating and/or stabilizing Mdm2 in a cell, comprising contacting the cell with HAUSP, in an amount effective to deubiquitinate and/or stabilize Mdm2, classified in class 435, subclass 4.

VII. Claims 47-49, 54-55 and 57-58, as specifically drawn to a method for identifying a modulator of Mdm2-HAUSP interaction, classified in class 435, subclass 4.

VIII. Claim 50 and 53, as specifically drawn to a modulator of Mdm2-HAUSP interaction, classified in class 530, subclass 350; 386.

IX. Claim 56, as specifically drawn to an agent that is reactive with Mdm2, classified in class 530, subclass 350; 386.

X. Claim 59, as specifically drawn to an agent that is reactive with HAUSP, classified in class 530, subclass 350; 386.

XI. Claim 60, as specifically drawn to a complex comprising Mdm2 and HAUSP, classified in class 530, subclass 350.

The inventions are distinct, each from the other because of the following reasons:

The inventions of Group I and Group II are directed to related methods for determining whether a subject has neoplasia comprising assaying a diagnostic sample of the subject for Mdm2 expression and HAUSP expression. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case,

each of the inventions detects Mdm2 and HAUSP expression using structurally and functionally distinct materials. For example, the method of Group I utilizes an antibody as compared to the method of Group II which utilizes a nucleic acid probe. As such, each method has a different mode of operation, which performs this function using structurally, and functionally divergent material. Therefore, each method is divergent in materials and steps. For these reasons the inventions of Groups I-II are patentably distinct.

Furthermore, the distinct steps and products require separate and distinct searches. The inventions of Groups I-II have a separate status in the art as shown by their different classifications. As such, it would be burdensome to search the inventions of Groups I-II.

The inventions of Group I-III are directed to related methods for determining whether a subject has neoplasia comprising assaying a diagnostic sample of the subject for Mdm2 expression and HAUSP expression. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, while each of the methods measure HAUSP and Mdm2 expression levels, the sample population from which the diagnostic sample is obtained represent separate and distinct populations with different morphologies and functions such that one population could not be interchanged with the other. As such, the instantly claimed methods are not obvious variants because each population would require different searches and consideration of different patentability issues.

The inventions of Groups V-VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the specification does not disclose that their methods would be used together. The method for treating neoplasia in a subject (Group V), the method for debiquitinating and/or stabilizing Mdm2 in a cell (Group VI) and the method for identifying a modulator of Mdm2-HAUSP interaction (Group VII) are unrelated as they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. Each invention performs this function using

structurally and functionally divergent material. Moreover, the methodology and materials necessary for detection, treatment, and modulation differ significantly for each of the materials. For identifying a modulator of Mdm2-HAUSP interaction, a cell is contacted with an agent and the interaction between Mdm2 and HAUSP is assessed. For debiquitinating and/or stabilizing Mdm2 in a cell, the cell is contacted with HAUSP. For the treatment of neoplasia, the agent is administered via any route of administration. Therefore, each method is divergent in materials and steps. For these reasons the inventions of Groups V-VII are patentably distinct.

Furthermore, the distinct steps and products require separate and distinct searches. The inventions of Groups V-VII have a separate status in the art as shown by their different classifications. As such, it would be burdensome to search the inventions of Groups V-VII.

The inventions of Group VIII and IX-X are directed to related agents which may interact with Mdm2 and/or HAUSP and disrupt Mdm2-HASUP interaction. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, while both compounds may interact with Mdm2, the invention of Group VIII does not specifically limit the interaction to only Mdm2 such that the modulator of Mdm2-HAUSP interaction may interact directly with HAUSP. As such, the inventions of Group VIII and IX are patentably distinct.

The inventions of Group VIII and Groups V, VII are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the modulator of Mdm2-HAUSP interaction can be used in a materially different process such as in vivo administration for the treatment of a disease or for the in vitro assessment of Mdm-2-HAUSP interaction.

The inventions of Group IV and Group I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the kit of Group IV can be used in a materially different process such as for the detection of neoplasia either an antibody or a nucleic acid which hybridizes to the nucleic acid encoding HAUSP or Mdm2.

Because the inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the search required for each group is not required for other groups because each group requires a different non-patent literature search due to each group comprising different products and/or method steps, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any

amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Note:

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF
5/11/2006

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER